

**FTS-NCI**

**Moderator: James Hadley**  
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James Hadley: Thank you operator. Good afternoon, ladies and gentlemen, and welcome to this call. I want to welcome you on behalf of the Food and Drug Administration, the National Cancer Institute and the Centers for Medicare and Medicaid Services.

Today's teleconference on the Oncology Biomarker Qualification Initiative (OBQI) marked the launch of a joint agreement between the FDA, NCI and CMS that will help improve the cancer therapy development process.

You will hear directly from the leadership of these agencies about this important collaboration and what it means to both patients and advocates.

With us today we have Dr. Andrew von Eschenbach Acting Commissioner at the Food and Drug Administration and Dr. Janet Woodcock, Deputy Commissioner for Operations at the FDA, Dr. Anna Barker, Deputy Director for Advanced Technologies and Strategic Partnerships at the National Cancer Institute and Dr. Peter Fox from the Centers for Medicare and Medicaid Services, and he's Senior Advisor in the Office of the Administrator at CMS.

We're going to open the program today with Dr. von Eschenbach. But before I do that, I do want to remind you that there is a news release on all three websites; [www.fda.gov](http://www.fda.gov), [www.cancer.gov](http://www.cancer.gov) and [www.cms.hhs.gov](http://www.cms.hhs.gov). Go to their news -- click on news -- and look at the press release there. Dr. von Eschenbach (unintelligible).

Andrew von Eschenbach, M.D.: Thank you, James. And welcome. It's a great privilege for the FDA to be able to host this very important discussion on the Oncology Biomarker Qualification Initiative.

And it's particularly important for advocates, as I believe this represents something that we have looked forward to and hoped for for a considerable period of time.

You're going to hear from Drs. Woodcock, Barker and Fox about the details of this important initiative, and specifically the impact that we believe that it's going to have on our ability to both develop and deliver more effective interventions for cancer patients.

But I want to take a moment at the very outset to put this into the important context that I believe we have been looking forward to and anticipating.

This is an opportunity for us to use biomarkers - the ability to now look at the molecular error from the perspective of finding new tools that will give us insight into the biologic effects of the treatments that we are developing and utilizing.

And then to be able to use that information to select appropriate patients for different interventions, to be able to determine in real time the effect of those interventions based on their biologic effects, and to be able to select

interventions with anticipation of not just their effectiveness, but assurances of their safety.

It's also an opportunity to bring together three important agencies within the federal government that are critical parts of this discovery, development and delivery continuum.

And for the three agencies to work effectively and collaboratively together to streamline and accelerate this process. To be able to move quickly from our understanding of fundamental mechanisms that underlie the problem of cancer to the development of solutions based on those molecular mechanisms, and then to be able to deliver those to patients in a way that the actual delivery gives us data and information about the proper utilization of those interventions.

And so really for us struggling and laboring to make a difference in the lives of patients threatened by cancer is an opportunity and a moment in which we can forge a new future in which patients need not suffer and die from cancer based on our ability to discover, develop, and deliver these more effective interventions using biomarkers as a key element in the foundation of how we can go about this process.

So I'm going to turn it back over to Mr. Hadley as we begin the discussion of the specifics by Drs. Woodcock, Barker, and Fox.

James Hadley: Thank you, Dr. von Eschenbach. We'd like to hear about the details of the program from Dr. Janet Woodcock, Deputy Commissioner for Operations at the FDA.

Janet Woodcock, M.D.: Thank you. This is basically a formation of a federal partnership to improve cancer treatment and prevention. That is the objective.

And the way we want to do that is by qualifying new cancer biomarkers. And of course by biomarkers, we mean tests of various kinds; everything from imaging to blood tests to tests on the tumor that will tell us something about how a patient is doing or what their prognosis is and so forth.

And by qualifying we mean doing the work that tells us what that test means. Does it predict something? Can it be used as a surrogate in trials and so forth?

And to give you some examples of the kind of biomarkers we think we're going to be looking at, we want to qualify biomarkers that tell us who is at high risk for getting a tumor, for example; a risk to our patient biomarker.

We'd like to study biomarkers that tell you which drug is going to work fast for your specific tumor; not just, say, one cancer as a group or breast cancer, but the specific cancer that you have as a patient, what is the best choice of drug that will give you the best response to your tumor.

And what about chance of recurrence after you've had treatment? Right now we look at populations, and we say this - after you've gone through this type of treatment you have a maybe 30% chance of recurring.

Well, who is in the 30%? We want to find that out. We want to identify those people. We want to treat them. And we don't want to treat the 70% of people who are at much lower risk of recurrence.

And same with safety. Who is at risk for side effects? We know right now for some cancer treatments that people who metabolize those drugs, who use

them slowly in the body, are at much higher risk for side effects. That makes a lot of sense. And we can right now, with a few tests, predict who is at risk and lower their dose.

We need to develop better tests qualified that are biomarkers to predict that risk to patients. These sets of activities and qualifying these biomarkers, they will then be able to be used in drug development to help inform us quickly about the performance of a drug product and assess whether or not it's effective and safe. And at the same time, these markers can then be translated into cancer practice and help personalize therapies for cancer patients much better.

Now, that's what we're trying to do. The structure of the initiative is as follows. We're pooling or sharing resources in leadership across those three federal agencies that are part of this partnership or initiative.

Obviously National Cancer Institute can contribute cutting edge science, but FDA knows what is in the regulatory pipeline and what our regulatory means are; what kind of markers are actually needed for development.

And CMS understands what evidence base is needed out in the real world of cancer treatment; what is needed to form the basis for reimbursement and so forth.

On the managerial side, we're coming together to organize federal priorities so that we have a coherent strategy taking into account the different needs I just talked about.

We have a coherent strategy for prioritizing what should be done based on the needs that are identified both by these agencies and their constituents. We can

also organize, and we plan to execute these projects by organizing various collaborations.

We're not just going to do them within the government. This is not the kind of activity generally that can be done in one sector. We plan to work across many sectors and we probably will bring in other federal agencies as appropriate.

So we also are viewing this as a resource pooling activity, where we pool - NCI brings to the table many, many federal trials in cancer and research activities in cancer. FDA brings our personnel to the table, and CMS brings access to many, many patients who are undergoing therapy and understanding their needs.

So in summary, we're setting up a collaboration that will both identify, prioritize, and then try to execute qualification of these cancer biomarkers that we think will really help patients in the end. Thank you. I'll turn it back to Mr. Hadley.

James Hadley: Thank you so much Dr. Woodcock. And now Dr. Anna Barker will discuss the significance of this program for both patients and advocates.

Anna Barker, Ph.D. :Thank you, James. And welcome everyone; thank you for joining us today. As you just heard from Dr. Woodcock, this is, I think, a partnership for scientists to patients- because we've been discussing the value of the science of biomarkers and talking a lot about it in the press and certainly supporting a lot of research through the National Cancer Institute, including a couple of large scale science projects, which we've discussed actually with this group, including the cancer genome atlas.

So we have a lot of investment in biomarker development. Biomarkers, as you know, are indicators of the physiology of cells and actually are good measures of all kinds of things, but most especially we're interested in them here in terms of measuring response to therapy.

And being able to use biomarkers, be they biochemical biomarkers such as proteins or genomics as I've just discussed or some of the technologies that we're talking about today, like imaging, for the evaluation of drugs in patients and to do some of the kinds of things that Dr. Woodcock has just talked about.

NCI brings to this an enormous wealth of science, and our goal is to leverage the science so that we have the very, very best evidence to bring forward to the agency and in collaboration with FDA and CMS. Design the kind of trials that answer very specific questions about biomarkers.

And this requires a bit of a system, actually. Moving from the science to the regulatory task - the critical task, which the FDA has defined now, will take us into some very specific answers that can be used by CMS to ultimately make their decisions based on hard scientific evidence.

So this is I think a great step for all of us in terms of really leveraging science for the benefit of patients, specifically around realizing the promise of biomarkers.

Now, the first initiative that we're going to undertake in this biomarker qualification initiative for oncology is an interesting one. And we've thought a lot about this in terms of where to begin this sort of blueprint that we're developing for how to actually qualify these biomarkers.

And we settled on a very interesting biomarker, which is FDG-PET, and I'm going to tell you what it means once, because you're never going to want to hear it again. But FDG-PET for those of you online who know this stands for fluorodeoxyglucose positron emission tomography.

We won't be asking you any more questions to repeat that, but FDG-PET is a very important technology for us in oncology, as many of you know, for assessing responsiveness to therapy, for looking at patients in a very critical way.

And it's a dynamic, functional imaging technology that allows us to measure certain changes in tumors.

FDG-PET specifically looks at the metabolism of glucose in tumors, which, as it turns out, is a very good measure of the metabolism of tumors and the extent to which tumors are active.

So we're using this physical parameter, which we now can quantify and standardize to look at responsiveness in non-Hodgkin's lymphoma. And so one of the first trials that we're going to develop and potentially begin to undertake this biomarker qualification with FDA and CMS is to use FDG-PET in non-Hodgkin's lymphoma, which is our - which we have about 50,000 to 60,000 new cases of this disease every year and it is a disease that's increasing, by the way.

But we believe that given that we have enormous databases in lymphoma overall, both Hodgkin's disease and non-Hodgkin's lymphoma that this is an extremely good place to start.

The data are quite strong. We can standardize and quantify our responses here. So we believe that the first couple of questions that will be asked by the experts in designing these trials will be to look at FDG-PET as an indicator of clinical outcome potentially, and also for early response to therapy.

The latter being the most likely; can we measure early responders with this approach? And there are other questions one could ask in lymphoma as well using FDG-PET.

Our process is going to be fairly straight-forward. We're going to identify - NCI and FDA and CMS - will identify the marker of interest, the disease of interest; we will determine the strength of the science in terms of whether or not we all, as a partnership, believe that this is a biomarker that can be measured very specifically in a specific disease.

We will bring a group of experts together to design the trial for qualification and then we'll proceed to do the trials. Some of the trials will be done through our current infrastructure. We can add on pieces to current trials as an example, through our cooperative groups.

Some of the trials will be done through consortia, that could be developed with groups of interest that have an interest in a specific disease, for example, or just an interest in drug development.

And we believe that this first trial in non-Hodgkin's lymphoma using FDG-PET will be an extremely good one to kind of set the stage for other diseases to follow.

And Dr. Woodcock may want to say more about this, but FDA and NCI have an interest across the board in many diseases and the use of imaging, specifically FDG-PET in those diseases.

So we think lymphoma is a great place to start, and we have had actually the support of your colleagues from the Leukemia Lymphoma Society in actually getting these experts together and it's a great way, I think, for the advocates to interface here and interact with us on developing these trials as we go forward and we have obviously other opportunities coming forward.

So I'll stop there, James, and thank you very much for allowing me to present this today.

James Hadley: Thank you so much, Dr. Barker. We don't have Dr. Fox on the line from CMS, and so we're going to go on. If he calls in, we will put him on the line. Right now, we would like to entertain some questions from the advocates. I want to remind you that the press release is on all three websites; fda.gov, cancer.gov and cms.gov. Click on news. Operator, could you queue us up for questions?

Coordinator: Thank you. At this time, if you would like to ask a question, please press star 1. You will be prompted to record your first and last name. To withdraw your question, press star 2.

Once again, if you would like to ask a question, please press star 1.

James Hadley: Again, I want to remind you that the websites at all three agencies; fda.gov, cancer.gov and cms.gov. Are there any questions?

Coordinator: (Carolina Hineirosa), you may ask your question.

(Carolina Hiestrosa): Thank you. Yes, I have two questions on this. What relationship does this initiative have with the PACT program within NCI? And also, what resources are being devoted to this whole effort?

Anna Barker: (Carolina), can you re-ask your first question?

(Carolina Hiestrosa): Yes. What relationship does this initiative have with the PACT program within NCI; the program for the assessment of clinical cancer tests we are familiar with? And then also what resources are going to be devoted to this initiative long-term?

And I understand that this is a collaboration between the three agencies, but I would like to also to know who else is participating in priority setting. Are you working with consumer groups and looking at certain criteria and priorities for this?

Anna Barker: Let me answer the last question first, which is basically - in terms of priority setting, the priority setting is based on science, and the extent to which FDA specifically and CMS as well have familiarity with, and we have data in certain - with certain of these biomarkers in selective diseases.

So it will be primarily based on the strength of the science. But as you heard from lymphoma -- the Leukemia Lymphoma Society -- as an example for this first trial, will be participating in the meeting of experts. And so that discussion will be a fairly broad discussion with experts from academia, the private sector, and the public sector, including FDA and CMS and NCI.

The resources, (Carolina), are primarily resources that are coming to our interagency oncology task force within the agencies right now. We believe,

though, that once we get this initiative up and running, we will be able to attract additional investment through consortia that would allow individual organizations and groups of organizations to participate to actually qualify specific biomarkers of interest.

And so there's - we'll be working through our current resource base through our interagency oncology task force, and through the clinical trials infrastructure of the NCI.

In terms of our relationship to the PACT organization; we don't have a formal relationship there. We basically- this FDA, NCI, CMS relationship -is purely directed toward the qualification of biomarkers. And so at this point, anyway, we haven't broadened it beyond that.

James Hadley: Thank you. Is there another question?

Coordinator: (Marilyn Eichner).

(Marilyn Eichner): Yes. My question is; are there going to be clinical trials open to children?

Anna Barker: That's a good question. And I don't think, you know, we're going to exclude any populations at this point. And as you know, we've been quite successful in clinical trials with children, but as you also know, we're getting (unintelligible) on recurrence of disease in children, so we are looking for ways to encourage especially the private sector to really reinitiate and/or accelerate many of their activities in terms of developing new drugs for children.

So I think if there is sufficient scientific evidence, if the trials are available, and if, in fact, we believe that there's real value in doing trials, we would open

up - yes, we would definitely open up those kinds of trials. Dr. Woodcock might want to say something about that.

Janet Woodcock: Yeah. Obviously, for pediatric cancer as well as for adult cancer, the more biomarkers that we can qualify and use, the more informed the development will be, the more confidence we'll have in the treatment.

Therefore, as Anna said, if there's enough evidence to undertake a qualification effort, we would want - we would certainly identify that and do it.

These qualification programs, though, need to be - we need to have a certainly amount of scientific evidence available on the biomarker before we start doing these in people. And we need to gather up that evidence and see how strong it is - how promising that marker is, because we then have an infinite number of subjects in order to do these efforts on, and we have to - we need to make sure we're focusing on the highest priority.

(Marilyn Eichner): Thank you.

Coordinator: (Hildy Dillon), you may ask your question.

(Hildy Dillon): Actually it's (Ed Barowski), who's with me here. He's in our information resource center.

(Ed Barowski): Hi. Dr. Barker, you had mentioned that this OBQI could be added to existing clinical trials. Would you be able to give us any examples of such trials that it could be added to?

Anna Barker: Not off the top of my head. We actually are - we have before selecting this lymphoma test - FDG test combination we did look across all the cooperative groups, and there are, as you probably know, a lot of trials are in lymphoma.

So we've asked our - internally we've asked our experts and there are apparently several trials that we could add on specific questions to. And we will be - we're convening a meeting on March 20 with the experts in leukemia and lymphoma, and at that meeting we'll be basically reviewing those trials and making those decisions.

Janet Woodcock: If I could add to that -- this is Janet Woodcock -- many of the trials we hope that we do -- many of the qualification efforts -- will be add-ons to existing programs that are going on either in the private sector and the public sector.

We hope to accomplish a lot of this by consortia across many different areas. We may not even have "formal trials." They may be treatments that are going on in healthcare settings and so forth where we could do the biomarker tests and then we could see if it correlated eventually with how well the people did and provided additional information.

So we're seeking a larger variety of venues where these biomarkers can be qualified, and we're trying to add this on to what exists out there rather than building some entire other structure to get this work done.

(Ed Barowski): Okay.

James Hadley: Are there any other questions?

Coordinator: (Robert Carroll).

(Robert Carroll): Yes; I have a two-part question. Are drug companies presently playing a role in this biomarker research? And is this research pretty much limited to the United States?

James Hadley: Dr. Woodcock?

Janet Woodcock: The answer to the first question, which is; are drug companies playing a role? The pharmaceutical industry over time has tried to develop biomarkers within the context of specific cancer drug development programs that they do.

And what we've concluded with talking to them is that probably isn't the best model. A lot of the drug development programs -- nine out of ten of them -- fail. And therefore it isn't a good way to be testing other things.

Also, we need more generalizability (sic). In other words, we need to see how the marker performs with a variety of treatments and a variety of patients, not just limited to one trial or one development program.

So what we've talked to pharmaceutical companies, device companies and other folks about is coming together in a variety of consortia where we all pool our resources together and we use whatever resources are available out there; perhaps assays that have been developed by the pharmaceutical companies, perhaps the data they have on FDG-PET and lymphoma they would be willing to donate.

And so we're trying to set up the venue starting with this announcement we're making today of the federal structure for this, whereby this information can be pooled to benefit everyone.

James Hadley: We only have time for one more question.

Coordinator: (Jim Omel).

(Jim Omel): Hi. I'm FDA patient rep and also with the CARRA [Consumer Advocates in Research and Related Activities] program. What are some of the other cancers in which biomarkers are close to being included in this cooperative initiative program?

Anna Barker: That's a good question. We have several, actually, that are on the list and just for FDG test for example, there are obviously several questions within lymphoma.

We don't, you know, we're going to have to structure our trials to make sure that we very specifically are asking the right questions so that we are able to answer it.

But areas like lung cancer is a good example. I think that anywhere that FDG-PET has been used in a robust way and we have a pretty good defined data set of information about the impact in that particular cancer. I think that cancer would actually be - certainly be a viable candidate for one of these demonstration trials. Dr. Woodcock may want to comment further.

Janet Woodcock: Yes. In addition, we're also of course very interested in other advanced imaging technologies. There are imaging technologies that look at vascularization, for example, of tumors, and how that responds to different treatments.

There are - and then there's a whole issue of blood tests or tests on the tumor itself. And we're, you know, working up all these. As Dr. Barker said, what we have to do is figure out the strength of the current scientific evidence.

And the way we want to pick these candidates out is to pick the ones - to pick the, you know, the low-hanging fruit, so to speak. We want to go for where we really think with an additional push with a big trial across the sector, pooling our resources, we can come out with something real that will benefit people very quickly.

James Hadley: Thank you so much. We're sorry we don't have time to answer all of your questions. However, on behalf of the FDA, NCI, and CMS, if you want to send us an email we'll try to get you an answer. We'll triage it to the other agencies. Please send that email to [liaison@od.nci.nih.gov](mailto:liaison@od.nci.nih.gov). One more time, [liaison@od.nci.nih.gov](mailto:liaison@od.nci.nih.gov).

I want to remind you one more time also that the news release is available at [fda.gov](http://fda.gov), [cancer.gov](http://cancer.gov) and [CMS.gov](http://CMS.gov). We thank each and every one of you for joining us today, and we certainly thank Dr. Barker, Dr. von Eschenbach, and Dr. Woodcock for bringing us up to date on this new initiative. Good afternoon ladies and gentlemen.

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